1206-80 **Mitral E Velocity Variation During Respiration in Patients With Heart Failure: Evidence for Pericardial Restraint?**

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Background: Pericardial restraint contributes to the diastolic filling abnormality in heart failure (HF). The presence or magnitude of respirophasic change in Doppler flow velocity curves may be helpful in demonstrating the existence of pericardial restraint.
Methods: We prospectively studied 113 pts with HF, left ventricular ejection fraction (LVEF) <50%, no clinical or 2D echocardiographic evidence for constrictive pericarditis (CP), and no history of chronic lung disease. Pulsed-wave Doppler interrogation of the mitral inflow was performed with simultaneous respiratory recording. The presence or absence of a third heart sound (S3) was determined by auscultation and confirmed by phonocardiography. Significant mitral E velocity variation (MEVV) was defined as a >25% increase during the first cardiac cycle coincident with the onset of expiration compared to the inspiratory cycle.
Results: Significant MEVV was present in 35 pts (31%). It was more frequently observed in pts with an audible S3 than in those without a S3 [13/26 (50%) vs. 22/87 (25%), P=0.017], and in pts with LVEF <30% compared to those with LVEF ≥30% [29/45 (39%) vs. 6/33 (17%), P=0.0093]. MEVV tended to be more common in pts with any degree of RV systolic dysfunction on 2D echocardiography [19/46 (41%) vs. 16/66 (24%), P=0.055). MEVV was not related to heart rate, respiratory rate, body mass index, the degree of MR, or left and right ventricular dimensions.
Conclusions: Significant MEVV was present in nearly 1/3 of pts with HF, especially those with severely reduced LVEF. The association with a S3 suggests a common basis in pericardial restraint. Isolated MEVV is an unreliable criterion for diagnosing CP in pts with HF and reduced EF.

1206-81 **The Beneficial Effect of Optimized Neurohormonal Therapy on Exercise Capacity in Heart Failure Patients Is Associated With the Restoration of Endothelial Function**

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Background: Improvement of exercise capacity in congestive heart failure (CHF) has been attributed to restoration of endothelial function. Angiotensin converting enzym inhibitors (ACEI) as well as Beta-blockers (BB) enhance endothelial function and exercise capacity in these patients. The role of endothelial function in short term improvement of functional status due to optimized neurohormonal inhibition in CHF is unknown.
Methods: In 33 patients with CHF (ejection fraction 24±8%) distance in 6-minute walk test, NYHA class, BNP, and flow-mediated vasodilation (FMD) of the brachial artery were evaluated at baseline and after a 3 months period where neurohormonal therapy was optimized. 2 groups were formed retrospectively according to the changes in functional status (responders and non-responders to optimized neurohormonal therapy).
Results: Responders (n=17) were characterized by an improvement in 6-minute walk test of at least 40 m (304±109 to 441±75 m; p<0.01), and a decrease in NYHA class (2.7±0.6 to 2.0±0.4; p<0.01) and BNP (484±454 to 243±197 pg/ml; p<0.01). No significant changes in walking distance (426± 97to 408±110 m; NS), NYHA class (2.4±0.7 to 2.1±0.9; NS) and BNP (299±313 to 236±215 pg/ml; NS) were seen in non-responders. At baseline age, gender, NYHA class, quality of life score, ejection fraction, left-ventricular enddiastolic diameter, heart rate, systolic blood pressure as well as dose of ACEI and BB were not significant different. Optimization of neurohormonal therapy (ACE-I and/or BB) during study period was comparable between groups. Improvement in functional status in responders was associated with an increase in FMD (8.2±3.9 to 11.0±5.6 %; p<0.05). In contrast, in non-responders FMD even slightly decreased (8.0±4.9 to 7.1±4.6 %; NS). Increase in walking distance was significantly correlated with improvement in FMD (r=0.34; p<0.05).
Conclusion: Short-term improvement of functional status in CHF patients following optimized neurohormonal therapy is associated with restoration of peripheral endothelial function. This results support the substantial contribution of peripheral vasculature to CHF.

POSTER SESSION

1207 Cardiomyopathy: Miscellaneous

Tuesday, April 01, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 4:00 p.m.-5:00 p.m.

1207-82 **The Role of Cardiovascular Magnetic Resonance in the Evaluation of Familial Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy**

Mohammad S. Hamid, Asifa Quraishi, Juan R. Gimeno, Rajesh Thaman, Anna Johns, Sami Firoozi, Perry M. Elliott, William J. McKenna, Dudley Pennell, St. George's Hospital Medical School, London, United Kingdom, Royal Brompton Hospital, London, United Kingdom

Background: Diagnosis of familial arrhythmogenic right ventricular dysplasia/ cardiomyopathy (ARVD/C) can be difficult due to variable penetrance and lack of a single diagnostic test. There are relatives with isolated abnormalities who do not fulfill ARVD Task Force criteria. We hypothesized that these findings represent disease expression and studied the role of cardiovascular magnetic resonance (CMR) in clarifying this.
Methods: First-degree relatives and 9 index cases had ECG, SAECG, echo, exercise testing and Holter. Relatives were grouped as affected (fulfill criteria), probable (isolated minor abnormalities) and unaffected and underwent CMR along with index cases.
Results: Sixty-one relatives (age 32 ±15 yrs, male 34%) were evaluated; affected 10(16%), probable 16(26%) and unaffected 35(58%). Abnormalities in the probable group were: ECG/SAECG 9(56%), echo 2(13%), ectopy>1000/24hr 4(25%)and NSVT 1(6%). CMR was abnormal in all index and affected cases with intramyocardial fat only identified in these cases. There was a difference in RV volumes between unaffected and probable ARVD (Table). Analysis showed that a 10 ml increase in RVEDV increased the probability of fulfilling diagnostic criteria by 1.5 and a WMA by 11.5.
Conclusion: The results of CMR support the hypothesis that minor abnormalities seen in ARVD relatives represent disease expression. CMR offers additional information when evaluating familial ARVD.

Results of CMR in Relatives of ARVD Patients

RELATIVES	UNAFFECTED (35)	PROBABLE (16)	AFFECTED (10)
Abnormal Echo	0	2 (13%)	5 (50%)
Abnormal CMR	0	6 (37%)	10 (100%)
RVEDV (mls)	140 ±36	157 ±46.6†	199 ±62‡
RVESV (mls)	59 ±20	76 ±27‡	106 ±48‡
RV Wall Motion Abnormality (WMA)	4 (11%)	6 (37%)	8 (80%)

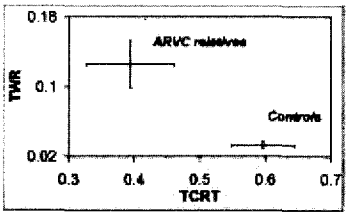
†p<0.05 (vs unaffected) ‡p<0.005 (vs unaffected)

1207-83 **Heterogeneity of Ventricular Repolarization Is Increased in First Degree Relatives of Patients With Arrhythmogenic Right Ventricular Cardiomyopathy**

Velislav N. Batchvarov, Mohammad S. Hamid, Katerina Hnatkova, Rajesh Thaman, Juan R. Gimeno, Peter Smetana, Sami Firoozi, Asifa Quaraishi, Perry M. Elliott, William J. McKenna, Marek Malik, St. George's Hospital Medical School, London, United Kingdom

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an autosomal dominant genetic disease with variable penetrance. We hypothesised that repolarisation abnormalities predisposing to arrhythmias might exist in asymptomatic relatives of ARVC patients.
Methods: Ten consecutive digital ECGs were recorded in each of 27 asymptomatic first-degree relatives of index ARVC cases (8 men, age 32±14 years) with normal 12-lead ECGs, and 27 age- and sex-matched healthy controls. Heart rate, QT interval, and QT dispersion (QTd) were measured automatically (QT Guard, GE Marquette). After singular value decomposition, repolarisation heterogeneity was quantified by TCRT (cosine of the spatial QRS-T angle, lower values signify increased repolarisation heterogeneity), and by the non-dipolar (i.e. not reflected in the heart vector) components of the T wave (T wave residua, TWR, proportion [%] of the whole T wave energy).
Results (mean±SEM): TCRT was significantly decreased whereas TWR were significantly increased in ARVC relatives compared to controls (TCRT: 0.39±0.07 vs 0.60±0.05, p=0.02, TWR: 0.13±0.03 vs 0.03±0.005%, p=0.002). Heart rate, QT interval and QTd did not differ significantly between relatives and controls. QTc was slightly longer in relatives with Bazett (415±5 vs 403±2 ms, p=0.02), but not with Fridericia formula (405±4 vs 396±2, p=0.07).

Conclusions: Despite normal ECG, repolarisation abnormalities predisposing to arrhythmias might exist in asymptomatic relatives of ARVC patients.



1207-84

Are Right Ventricular Wall Motion Abnormalities Reliable for the Diagnosis of Arrhythmogenic Right Ventricular Cardiomyopathy? A Cardiac Magnetic Resonance Imaging Study in Healthy Subjects Using a New Segmental Model

Burkhard Sievers, Ulrich Franken, Marvin Addo, Asli Bakan, Simon Kirchberg, Hans-Joachim Trappe, University of Bochum, Herne, Germany

Aims: To evaluate right ventricular wall motion abnormalities in healthy individuals using a new segmental model for the right ventricle.

Methods and results: 29 healthy individuals (9 female, 20 male, mean age 48.9±15 years) underwent magnetic resonance imaging (1.5 Tesla MRI Sonata, Siemens, Erlangen, Germany) to evaluate cardiac function and identify possible right ventricular wall motion abnormalities. TrueFISP gradient-echo sequences with steady-state free precession were used for image acquisition. Right ventricular wall motion abnormalities were analysed and classified according to a segmental model for the right ventricle. In 27 (93.1%) of the 29 individuals right ventricular wall motion abnormalities were found. Dyskinesia was found in 22 (75.9%), hypokinesia in 11 (37.9%) and bulging in eight individuals (27.6%). The number of diagnosed wall motion abnormalities in the transverse plane (86.2%) was significantly higher compared to those found in the short axis plane (13.8%) or in the horizontal longitudinal plane (41.4%) (p=0.000).

Conclusion:

Right ventricular wall abnormalities can be found in healthy individuals. Since these wall abnormalities are a criterion for the diagnosis of arrhythmogenic right ventricular cardiomyopathy, wall motion abnormalities around the insertion of the muscular ligaments of the right ventricle should be excluded to prevent an incorrectly positive diagnosis.

1207-85

Diastolic Dysfunction After Neurocardiogenic Injury: Prevalence and Association With Pulmonary Edema

Alexander Kopelnik, Poyee P. Tung, Nader M. Banki, Michael T. Lawton, Daryl Gress, Barbara J. Drew, Elyse Foster, William W. Parmley, Jonathan G. Zaroff, UCSF, San Francisco, CA

Introduction: ECG changes, troponin release, and reduced left ventricular ejection fraction (LVEF) have been described after subarachnoid hemorrhage (SAH). Little is known about the occurrence of diastolic dysfunction in this patient population. We aimed to determine the prevalence of diastolic dysfunction and its association with cardiac outcomes after SAH.

Methods: Over a period of 2 years, echocardiographic, clinical, chest X-ray, and cardiac troponin I (cTi) data was obtained on day 1, 3, and 6 following enrollment in consecutive SAH patients admitted to UCSF medical center. Each echocardiogram included Doppler recordings of mitral inflow (early[E] and atrial contraction[A] velocities, E wave deceleration time[DT]) and pulmonary venous flow (systolic[S] and diastolic[D] velocities). For each study, diastolic function was categorized as normal (E/A>1, S/D>1), impaired relaxation (E/A<1, S/D>1), pseudonormal (E/A>1, S/D<1, DT>150, age>40), or restrictive (E/A>1, S/D<1, DT<150, age>40). Subjects under 40 were included in the pseudonormal or restrictive groups if E/A>2 or S/D<0.4. LVEF was calculated by a blinded observer. Cardiac outcomes were treated as dichotomous variables: pulmonary edema by CXR (no or yes), LVEF (≥50% or <50%), and cTi (≤1.0 or >1.0 ug/L).

Results: The study included 173 subjects, 154 had technically adequate Doppler data. Diastolic dysfunction was observed on at least one echocardiogram in 68% of subjects. The prevalence of diastolic vs. systolic dysfunction in 25 patients with pulmonary edema was 84% vs 36% respectively (p=0.001 by chi square). A history of hypertension was significantly associated with all three categories of diastolic dysfunction. The restrictive pattern was associated with the following endpoints (by logistic regression): pulmonary edema (odds ratio [OR] 7.5; 95% confidence intervals [CI] 1.83 - 40.4; p<0.015); reduced LVEF (OR 12.9; 95% CI 2.68 - 61.87; p<0.001) and troponin release (OR 8.6; 95% CI 2.01 - 40.21; p<0.006).

Conclusions: Diastolic dysfunction is common in patients with SAH. It is associated with adverse cardiac outcomes and may explain the development of pulmonary edema in some SAH patients.

1207-86

Impact of Alpha-Tocopherol on the Hypertrophied Heart in a Murine Model of Systemic Carnitine Deficiency: The Involvement of 1,2-Diacylglycerol

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Background: The juvenile visceral steatosis (JVS) mouse, a murine model of systemic carnitine deficiency, shows disorder of fatty acid oxidation and develops cardiac hypertrophy associated with lipid accumulation. Recently, inhibitory effect of alpha-tocopherol (AT) on 1,2-diacylglycerol (DAG), which is independent of its antioxidant properties, has been reported. We investigated the involvement of DAG in cardiac hypertrophy due to fatty acid oxidation disorder by evaluating the effect of AT administration on the hearts of JVS mice.

Methods: Both JVS and control mice were fed a high AT diet or a standard diet from 4 to 8 weeks of age. Myocardial DAG level and its fatty acid composition were assessed at 8 weeks of age.

Results: The ventricular to body weight ratio in the JVS mice was significantly higher than that in the control mice (11.2 versus 3.8 mg/g, P<0.01), and was reduced by AT treatment (9.7 mg/g, P<0.05 versus JVS mice). Morphological analysis showed significantly increased ventricular wall thickness and myocyte width in the JVS mice compared with those in the control mice (P<0.01). AT treatment also significantly reduced them. In contrast, echocardiographic analysis showed deterioration of fractional shortening and exaggeration of left ventricular dilatation in the AT treated JVS mice (P<0.01 versus JVS mice). The myocardial thiobarbituric acid-reactive substance level, an index of oxidative stress, was not affected by AT treatment. The myocardial DAG level was 2.5-fold higher in the JVS mice (2004 versus 806 ng/ventricular weight, P<0.01) with a significant increase in fatty acids of 18:1 and 18:2 compared with that in the control mice. AT treatment reduced the myocardial DAG level in the JVS mice (1443 ng/ventricular weight, P<0.01 versus JVS mice) without any alteration of fatty acid composition.

Conclusions: AT treatment may partially reduce the cardiac hypertrophy but deteriorate the cardiac contractile function of JVS mice through the inhibitory effect on DAG. An increase in DAG level might be involved in the development of cardiac hypertrophy and in the maintenance of cardiac function in hearts with fatty acid oxidation disorder.

1207-87

Cardiovascular Manifestations in Females With Anderson-Fabry Disease

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Aims: Anderson-Fabry disease (AFD) is an X-linked recessive disorder. Recent data have shown that cardiac involvement in males is common, however, the prevalence of cardiovascular abnormalities in females is uncertain. The aim of this study was to characterise the cardiac structure and function in female patients referred for family screening or for cardiac assessment.

Methods: Fifteen female heterozygotes (mean age 53.3 ± 14.9 years, range 24-81) were identified either by mutational analysis or plasma α-galactosidase A (α-Gal) activity (mean 3.8 nmol/hr/ml ± 1.19, range 1.6-6.6nmol/hr/ml). All patients had an ECG and 2-D transthoracic echocardiography. Twelve patients were able to perform maximal cardiopulmonary exercise testing.

Results: Eleven of the 15 patients presented ≥ 40 years (mean 55 years ± 11.14, range 40-78) with cardiac symptoms. Four patients had hypertension. Thirteen patients had abnormal ECG's: short PR interval (n=2), Romhilt-Estes criteria for left ventricular hypertrophy (n=5) and T wave changes (n=13). Left ventricular cavity dimensions and aortic root diameters were normal in all patients. Eleven patients had valvular abnormalities; 11 patients had an increased left ventricular mass index (≥110g/m^2) mean 133.3g/m^2 ± 37.88, range 96-245g/m^2; 4 patients had septal hypertrophy (18.8mm ± 5.62, range 13-26mm). On transmitral Doppler, 5 patients had impaired relaxation with a reversal of their E/A ratio, and 1 patient had a restrictive left ventricular Doppler filling pattern. One patient had a low peak oxygen consumption ≤ 80% predicted on metabolic exercise testing.

Conclusion: This study suggests that cardiac involvement in females with Anderson-Fabry disease may be more common than previously reported.

1207-88

Presentation and Outcomes of Left Ventricular Noncompaction in Children

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Background: Better imaging modalities are contributing to increased awareness of left ventricular non-compaction (LVNC), but the significance of the diagnosis is often uncertain. This study describes our experience of LVNC in paediatric patients seen at the Royal Children's Hospital, Melbourne, the sole paediatric cardiology service for a population of 4 million.

Method: LVNC was diagnosed when prominent trabeculation of the LV involved greater than 50% of the myocardial wall on a short axis view (echocardiography or angiography). The clinical charts of all children exhibiting this characteristic myocardial anomaly were reviewed. Children referred for cardiac transplantation were excluded to avoid bias in the survival analysis.

Results: 54 children fitted the diagnostic criteria. 22 (13 male) had isolated LVNC and 32 (13 male) had LVNC associated with other congenital cardiac malformations (LVNC+CHD). These included hypoplastic right heart syndromes, atrial or ventricular septal defects, tetralogy or pulmonary atresia with VSD, truncus arteriosus and left heart obstructive lesions. Children with isolated LVNC presented later (5 months vs 2 days, p<0.001), were more likely to present with congestive cardiac failure (13/22 vs 6/32, p<0.01), and less likely to survive to five years of age (58% vs 88%, p<0.01) than those with LVNC+CHD. Death was sudden or unexpected in four patients and a result of progressive congestive failure in nine. A defibrillator was indicated for ventricular arrhythmias in one patient with isolated LVNC. LV systolic dysfunction or restrictive physiology was more common among survivors with isolated LVNC (10/14 vs 6/27, p<0.001).

Conclusion: Isolated LVNC is associated with higher mortality and worse long-term outcome than LVNC+CHD. Prospective studies may further illuminate the natural history of this unusual cardiomyopathy.